Value of perinatal necropsy examination

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SUMMARY   In a retrospective study of 150 stillbirths and 150 neonatal deaths carried out between 1981 and 1985 the necropsy findings were compared with the clinical diagnoses, which had been obtained from the postmortem request form, and the case notes completed before the necropsy was performed. In all cases the necropsy comprised macroscopic findings and histological examination of all organs, with microbiology, radiology, and cytogenetics where appropriate. Clinically important differences between clinical and pathological diagnoses in 54 of 150 cases (36%) were noted in the cases of stillbirth. Of the neonatal deaths, examination showed clinically important information that had not been recognised during life in 66 cases (44%). Histological examination of tissues was essential for making or confirming the pathological diagnosis in 20% of all perinatal deaths.

It is often erroneously assumed that diagnostic accuracy has been improved by the increasing refinement of medical investigation.[1] Furthermore, invasive investigations and more active management are likely to produce more side effects. These problems are found as often in neonates as they are in adults. In recent years there has been a steady decline in the number of necropsies performed on adults, apart from those of a medicolegal nature.

Most studies on the value of necropsy as an instrument of quality control have looked at adults, and there is a wide variation in results obtained in Europe and the United States. This is explained in part by the difference between necropsy rates and by different methods of study. In Sweden, where necropsies are performed on all hospital deaths unless the relatives object, Britton[2] found that the main diagnosis was confirmed in 57% of cases (necropsy rate 96%). Two studies in the United Kingdom have shown confirmation of the main diagnosis in 61%[4] (necropsy rate 25%) and complete agreement between the clinical and pathological diagnoses in 47% of necropsies[4] (necropsy rate 16%). In the United States Friederici and Sebastion[5] found that the main diagnosis was correct in 90% of cases but that diagnoses were completely confirmed in only 36% of necropsies. Goldman *et al*[1] in Boston looked at the value of necropsy in three different decades and found remarkably little change between 1960, 1970, and 1980. Despite dramatic changes in medical techniques of investigation and treatment in each of the three years examined

10% of necropsies showed major pathological abnormalities, which, if recognised before death, would have led to changes in management and perhaps to longer survival.

In the United Kingdom the necropsy rate in the perinatal period is generally much higher than that in adults. At Oxford over 90% of neonatal deaths and about 85% of stillbirths come to necropsy. As a result more complete information is available, giving the audit a greater value than that of the adult population. Despite this there has been little recently published work on the value of the necropsy in the perinatal period. In a retrospective study of 43 stillbirths and 35 neonatal deaths undertaken in a district general hospital[6] there was complete agreement between clinical and pathological diagnoses in 76% of cases. Additional pathological abnormalities were found in 13% of necropsies, and in the remaining 11% the pathological findings did not support the clinical diagnosis. In a second study in a teaching hospital[7] the same author found discordance between clinical and pathological diagnoses in 21% and additional information in 23% of necropsies.

Material and methods

In this study we looked at 150 neonatal deaths and 150 stillbirths, occurring between 1981 and 1985, and compared clinical diagnoses and necropsy findings.

To eliminate the retrospective rationalisation that often creeps in once necropsy findings are known the clinical diagnoses used were opinions expressed by clinicians in writing on a structured postmortem

request form and in the case notes before necropsy was carried out. In all cases necropsy findings included gross and histological examination of all organs, with microbiology, radiology, and cyto-genetics, where appropriate, because of the history of macroscopic findings.

The cases were classified into groups: (A) those where there was complete agreement between the clin-ical and pathological diagnoses; (B) those where there was disagreement; (C) and those where there was agreement on major problems but in which necropsy provided additional information. To determine the practical importance of the discrepancies found cases in groups B and C were further divided into those where there were implications for management of either the individual or unit, or where there were implications for counselling of parents contemplating future pregnancies, and those where pathological findings were without clinical importance at the present time.

We identified certain clinically important condi-tions for more detailed scrutiny. These were intra-ventricular haemorrhage and infection in neonatal deaths, intrauterine growth retardation (IUGR) in stillbirths, and major congenital anomaly in all peri-natal deaths.

Results

STILLBIRTHS

In 60 of the 150 stillbirths (40%) there was complete agreement between the clinical and pathological diag-noses; most of these (40) were antepartum deaths with or without signs of asphyxia for which no underlying cause was found. Another major abnormality in this group was placental abruption (n = 13). There was additional information from the necropsy in 51 cases (34%) and disagreement with the clinical diagnosis in

Table 1   *Clinical v pathological diagnosis*

	Stillbirths (%)	Neonatal deaths (%)
Agree	60 (40)	28 (19)
Additional information	51 (34)	99 (66)
Disagree	39 (26)	23 (15)

Table 3   *Underdiagnosed major congenital anomalies*

Stillbirths	Neonatal deaths
Atrial septal defect, ventricular septal defect, unilateral pulmonary agenesis	Cystic dysplastic kidneys
Potter's syndrome	Cystic dysplastic kidneys, hypoplastic lungs
Achondroplasia	
Transposition of great vessels	Complex cardiac anomalies
Duodenal atresia	Renal abnormalities, partial anomalous pulmonary venous drainage

39 cases (26%) (table 1). Table 2 shows the numbers indicating implications for management, counselling, or both. Major congenital abnormalities were both underdiagnosed and overdiagnosed, as well as misdi-agnosed (tables 3, 4, and 5).

Intrauterine growth retardation was missed clin-ically in 15 of the 150 stillbirths. Major placental infarction (20% or more of the placenta affected) was present in 15 of the cases in which pathological findings had implications for clinical management. Several of these comprised the same pregnancies in which IUGR had been missed. In the group with implications for counselling there were seven babies with cardiac anomalies and two each with hydrops fetalis, renal anomalies, and multiple abnormalities.

Histological examination of the tissues was required for diagnosis in 18 of the 90 cases (20%) where the necropsy findings did not completely agree with the clinical diagnosis. Eleven of the 18 fetuses were normally formed, and in nine of these the pathol-ogical abnormality was unsuspected infection. Three of the seven fetuses that were abnormal on gross examination had hydrops fetalis.

In total, there were implications for clinical action derived exclusively from necropsy information in 54 of 150 stillbirths (36%).

NEONATAL DEATHS

There was agreement between the pathological and clinical diagnoses in 28 cases (19%), additional infor-mation was provided by the necropsy in 99 (66%), and there was disagreement in 23 (15%) (table 1). Where there was agreement, prematurity and its com-

Table 2   *Implications for clinical action*

	Stillbirths				Neonatal deaths		
	Additional information	Disagree	Total		Additional information	Disagree	Total
Management	17	14	31		38	8	46
Counselling	12	7	19		8	4	12
Both	2	2	4		1	7	8
Neither	20	16	36		52	4	56
Total	51	39	90		99	23	122

Table 4 *Misdiagnosed major congenital anomalies*

Clinical diagnosis	Pathological diagnosis
Stillbirths:	
Multiple abnormalities	Amnion rupture sequence
Neonatal deaths:	
Osteogenesis imperfecta	Achondrogenesis type II
Occipital encephalocoele, renal abnormalities (2 cases)	Meckel-Grüber syndrome
Cerebral haemorrhage	Congenital primitive neuroectodermal tumour
Phocomelia, rectal agenesis, hypoplastic left lung, IUGR	VACTERL association
Trisomy 13	Pseudodicentric isochromosome 18
Cystic hygroma	Congenital cervical teratoma

Table 5 *Overdiagnosed major congenital anomalies*

Clinical diagnosis	Pathological diagnosis
Stillbirths:	
Hydrocephaly	Maceration
Hydrops fetalis, ? Fallot's tetrad	Maceration
Hydrops fetalis	Maceration
Neonatal deaths:	
Anomalous pulmonary venous drainage	Prematurity, pulmonary oedema, and haemorrhage
Congenital heart disease	Prematurity
Cyanotic heart disease, hydrops fetalis	Prematurity, hydrops fetalis
Cyst of fourth ventricle	Prematurity and its complications
Fetal abnormality	Prematurity

plications formed the largest group (15 cases or 10%), followed by major congenital anomalies (nine cases or 6%). Table 2 shows the figures for implications for management, counselling, or both, in B and C. As with the stillbirths, major congenital anomalies were underdiagnosed, overdiagnosed, and misdiagnosed (tables 3–5).

Intraventricular haemorrhage was missed clinically in 13 babies and overdiagnosed in eight babies. In a further seven infants intraventricular haemorrhage was suspected but was not definitely diagnosed. Infection was missed or treatment started too late to be effective in 16 babies.

Histological examination was essential for the diagnosis in 25 of the 122 cases (20%) in groups B and C. Eighteen of the babies were normally formed, and in 13 of these the pathological diagnosis was unsuspected infection. In total, there were implications for clinical action derived exclusively from necropsy information in 66 of 150 neonatal deaths (44%).

Discussion

The justification for necropsy examination in adults is usually cited as medical audit, medical education, and accurate death certification. These reasons apply equally for necropsies carried out in the perinatal period, but here additional information may be gained that is important for management of future pregnancies. With the fall in perinatal mortality rates there has been a relative increase in the number of deaths due to major chromosomal and congenital abnormalities, and the accurate diagnosis of these disorders is extremely important for the parents and siblings of a baby who has died. In some cases the information is relevant for counselling more distant relatives.

As would be expected, the necropsy showed less extra information about stillborn babies than neonatal deaths due to the considerable number of antepartum deaths with signs of asphyxia—but where the pathologist could find no underlying cause. Most pathologists and obstetricians believe that it is a waste of time to perform necropsies on macerated stillbirths. A recent survey of necropsies on macerated stillbirths carried out over 10 years in Oxford showed pathological abnormalities in 70 of 220 (32%) normally formed fetuses and in 114 (52%) of their placentae. In the same period 33 (15%) macerated stillbirths had major malformations.[8] The value of performing these necropsies is shown by a case in the present study of a fetus with hydrocephaly. Discovery of multiple cardiac rhabdomyomata prompted careful study of the fixed brain, which was poorly preserved due to maceration and hydrocephaly. This was rewarded by finding a tuber characteristic of tuberous sclerosis, a condition that often occurs as a result of a spontaneous mutation but is inherited in an autosomal dominant fashion, and signs in the parents may be found only after a deliberate search.

Of the major congenital abnormalities that were not identified until necropsy, a case of achondroplasia and a baby with Potter's syndrome might have been diagnosed prenatally with high resolution ultrasound scanning at the appropriate gestation. The other malformations, however, would have been difficult to pick up, even if they had been specifically sought, and necropsy was clearly an essential investigation in these cases. The overdiagnosis in macerated stillbirths of both hydrocephaly and hydrops fetalis due to deformation of the head or accumulation of fluid after death are well known pitfalls for those unfamiliar with the changes that occur after fetal death. Early amnion rupture sequence causes a bizarre collection of unusual major abnormalities in the fetus, and it is the asymmetrical distribution and combination of abnormalities which suggest the diagnosis, even when amniotic bands have disappeared. In this case obvious external abnormalities were noted at delivery, but their importance was not appreciated. The risk of recurrence is almost negligible, so accurate diagnosis

is necessary for correct counselling of the parents.

Of the stillbirth necropsies with implications for management, intrauterine growth retardation was missed in 15 pregnancies (10% of stillbirths). This is an important obstetric complication associated with intrauterine death and neonatal problems and may recur in subsequent pregnancies.[9] In several of these major placental infarction was present as well; this was also found in other cases in the absence of IUGR.

Mueller *et al*[10] proposed a protocol for making perinatal necropsies more cost effective. They recommended that histological examination should not be undertaken on all cases, and in particular, that it added little to the information gained from gross examination when the fetus was normally formed. In non-immunological hydrops fetalis they recommended karyotyping but not histological assessment. In this study the pathological diagnosis was partly or wholly reached after histological examination of the tissues in 20% of stillbirths, and histology was helpful in almost twice as many normally formed fetuses as in those that were abnormal on gross examination.

Three of the seven abnormal looking fetuses were hydropic; histological examination elucidated the underlying cause when a cardiac conduction system abnormality, cardiac rhabdomyomata, and myocarditis were identified.

Of the normally formed fetuses, unsuspected infection was the predominant pathological finding. Mueller *et al*[10] recommended bacterial culture in all perinatal deaths, although infections due to viruses and fungi would go undetected. Although specific organisms are only occasionally identified histologically, the method is less unreliable than culture for the unequivocal demonstration of infection.

Of the neonatal deaths, complete disagreement between the clinical and pathological diagnoses occurred less often than it did among stillbirths. Additional information, however, was provided more often by necropsy, and in almost half the neonatal deaths there were positive implications for clinical management.

In retrospect, all the major congenital abnormalities that were missed could have been diagnosed during life had the right equipment and expertise been available at the right time. Total anomalous pulmonary venous drainage is a notoriously difficult diagnosis to make clinically, and pulmonary oedema and haemorrhage were overinterpreted in one case in the present study. The remaining four babies in which a major congenital abnormality was overdiagnosed were all premature but normally formed. Both the VACTERL association (vertebral anal cardiac tracheoesophageal radial or limb defect) and pseudodicentric isochromosome 18 could have been diagnosed during life had the babies lived long enough

for the appropriate investigations to be performed. One of the babies with Meckel-Grüber syndrome had post-axial polydactyly of both hands and feet, which, in addition to the encephalocoele and renal abnormalities, made the diagnosis certain. In the remaining discrepant cases histological examination was required to make or confirm the diagnosis. Included in this group was a baby with a cerebral congenital primitive neuroectodermal tumour, which was clinically unsuspected and not identified during gross necropsy. Ultrasound scan of the baby's head had suggested an unusual cerebral haemorrhage; considerable haemorrhage had occurred within the very vascular tumour.

Ultrasound equipment for scanning the heads of premature babies for intraventricular haemorrhage became available in Oxford at about the beginning of the study. Until the medical staff had gained sufficient experience with it to make confident diagnoses, however, such results were not recorded in the case notes, and opinions expressed concerning intraventricular haemorrhage were made only on clinical grounds. Ultrasound scanning was not in routine use in Oxford until halfway through the study, and some hospitals in the region still do not have this facility. It is not surprising that intraventricular haemorrhage was missed in 13 babies, overdiagnosed in eight babies, and suspected but not firmly diagnosed in seven. These findings underline the need for such equipment to be available in all special and intensive care nurseries so that appropriate management can be started immediately.

Of the neonatal deaths, histological examination was essential for diagnosis in 20% of cases where this was changed or completed by necropsy. In common with the stillbirth group, histological examination was required for diagnosis in twice as many normally formed babies as malformed babies, showing unsuspected infection in most cases. Of the malformed babies, two had fetal hydrops; one due to cerebral arteriovenous malformation and the other to multiple hepatic vascular harmartomata.

This study has shown that necropsy completed or changed the clinical diagnosis in 212 of 300 perinatal deaths (70%) and that in 120 (40%) of the cases information obtained at necropsy was clinically important. In the 30% of cases in which such information did not affect clinical management or counselling it is, of course, still important for audit, education, and accurate death certification. Mueller *et al*[10] suggested that Potter's syndrome was the only indication for routine histological examination; this study has shown its value in 20% of perinatal deaths, two thirds of this group being normally formed babies. If histological examination is done only in selected cases then much useful information will be missed. Standard sampling

of tissues for histological examination should be a routine part of every perinatal necropsy.

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